

Harmonization and Communication of PBPK Models Using the Exposure-Related Dose Estimation Model (ERDEM) System: Trichloroethylene

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In support of the risk assessment for trichloroethylene (TCE), NERL and NCEA are developing an updated, physiologically based pharmacokinetic (PBPK) model. The PBPK modeling effort is in conjunction with a workgroup organized by TERA (Toxicology Excellence for Risk Assessment) that includes researchers from academia, the Air Force, and outside industry. PBPK models are powerful computational tools that can be used to link exposure to the internal exposure dose or concentrations of parent compounds and/or active metabolites at the target site(s) of toxicity. Challenges in model development are the comparison and harmonization of existing models, management of multiple diverse datasets, and characterizing the uncertainties. The implementation and documentation of a mathematical model in a general structure addresses these issues by managing the chemicals, compartments, and parameters in a consistent manner. The Exposure Related Dose Estimating Model (ERDEM) platform, developed by NERL, provides an appropriate structure. Also, the EPA Science Advisory Board has stressed the importance of transparency in the updated assessment of TCE. The development of the updated PBPK model in the ERDEM system addresses this charge through its graphical user interface (GUI), standard report generation, and availability to the public. Evaluation of the model can be done at a high level—standard reports or simulations of new scenarios through the GUI—and at varying levels of detail down to the actual FORTRAN code. This enables use and review by researchers of diverse backgrounds.